Application No. 09/859,503

$$\begin{array}{c|c}
R_1 & O & R_2 \\
O & N & N & R \\
CH_3 & R_4
\end{array}$$
or
$$H_3C$$

$$H_3C$$

$$O & R_2$$

$$O & R_2$$

$$O & N & N & R$$

$$CH_3$$
wherein:

 R_1 is selected from a member of the group consisting of hydrogen, hydroxyl, methoxyl, acylamino group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl (mercapto), sulfeno, sulfanilyl, sulfamyl, sulfamino, and phosphino, phosphinyl, phospho, phosphono and $-NR_aR_b$, wherein each of R_a and R_b may be the same or different and each is selected from the group consisting of hydrogen and optionally substituted: $C_{(1\cdot 20)}$ alkyl, $C_{(3\cdot 12)}$ cycloalkyl, $C_{(1\cdot 20)}$ alkenyl, $C_{(3\cdot 12)}$ cycloalkenyl, $C_{(1\cdot 20)}$ alkynyl, aryl, heteroaryl, and heterocyclic group;

 R_2 and R_3 are independently selected from a member of the group consisting of halo, thio, oxo, haloalkyl, alkoxyalkyl, $C_{(1-20)}$ alkyl, $C_{(1-20)}$ hydroxyalkyl, $C_{(1-20)}$ thioalkyl, $C_{(1-20)}$ alkylthio, $C_{(1-20)}$ alkylaminoalkyl, $C_{(1-20)}$ aminoalkyl, $C_{(1-20)}$ aminoalkyl, $C_{(1-20)}$ aminoalkyl, $C_{(1-20)}$ aminoalkyl, $C_{(1-20)}$ atiaminoalkyl, $C_{(1-20)}$ atiaminoalkyl, $C_{(1-20)}$ atiaminoalkyl, $C_{(1-20)}$ atiaminoalkyl, $C_{(1-20)}$ atiaminoalkyl, $C_{(1-20)}$ alkylamidoalkyl, $C_{(1-20)}$ amidoalkyl, $C_{(1-20)}$ acetamidoalkyl, $C_{(1-20)}$ alkenyl, $C_{(1-20)}$ alkylyl, $C_{(1-20)}$ alkoxyl, $C_{(1-20)}$ alkoxyl, $C_{(1-20)}$ alkoxyl, $C_{(1-20)}$ alkoxyl, $C_{(1-20)}$ alkoxyl, $C_{(1-20)}$ alkoxyl, and -NR_aR_b; and

Application No. 09/859,503

 R_4 may be hydrogen or an optionally substituted member of the group consisting of $C_{(1-20)}$ alkyl, $C_{(3-12)}$ cycloalkyl, $C_{(3-12)}$ cycloalkenyl, $C_{(1-20)}$ alkynyl, aryl, heteroaryl, and heterocyclic group.

4. (Amended) The therapeutic compound of claim 37, wherein each of R_2 and R_3 is substituted with one or more members of the group consisting of hydroxyl, methyl, carboxyl, furyl, furfuryl, biotinyl, phenyl, naphthyl, amino group, amido group, carbamoyl group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl, sulfeno, sulfanilyl, sulfamyl, sulfamino, phosphino, phosphinyl, phospho, phosphono, N-OH, $-\text{Si}(\text{CH}_3)_3$, $C_{(1-3)}$ alkyl, $C_{(1-3)}$ hydroxyalkyl, $C_{(1-3)}$ thioalkyl, $C_{(1-3)}$ alkylamino, benzyldihydrocinnamoyl group, benzoyldihydrocinnamido group, optionally substituted heterocyclic group and optionally substituted carbocyclic group.

5 U/2

(Amended) The therapeutic compound of claim 4, wherein the heterocyclic group 6. is a member selected from the group consisting of acridinyl, aziridinyl, azocinyl, azepinyl, benzimidazolyl, benzodioxolanyl, benzofuranyl, benzothiophenyl, carbazole, 4a H-carbazole, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, dioxoindolyl, furazanyl, furyl, furfuryl, imidazolidinyl, imidazolinyl, imidazolyl, M-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, noxpinanyl, octahydroisoquinolinyl, oxazolidinyl, oxazolyl, oxiranyl, perimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, 4pipendonyl, piperidyl, pteridinyl, purinyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyndinyl, pyridyl, pyndyl, pyndinyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolonyl, pyrrolyl, 2H-pyrrolyl, quinazolinyl, 4H-quinolizinyl, quinolinyl, quinoxalinyl, quinuclidinyl, β-carbolinyl, tetrahydrofuranyl, tetrahydrofsoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 2H-,6H-1,5,2-dithiazinyl, thianthrenyl, thiazolyl, thienyl, thiophenyl, triazinyl, xanthenyl and xanthinyl.

- 19. (Amended) A method for inhibiting an activity mediated by a cytokine, the method comprising:
 - (a) contacting cytokine responsive cells with a compound as defined in claim 1; and
- (b) determining that the cellular process or activity mediated by the cytokine is inhibited.
- A (Amended) The method of claim 33, wherein said disease is asthma.
 - 36. (Amended) A method for treating NIDDM comprising a step of administering to a subject in need of such treatment a therapeutically effective amount of a compound of claim 1.

Please add the following new claim:

37. (New) A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having one of the following formulae:

$$R_1$$
 R_2
 R_3
 R_4
 R_3
 R_4
 R_3
 R_4
 R_3
 R_4
 R_4

wherein:

 R_1 is selected from a member of the group consisting of hydrogen, hydroxyl, methoxyl, acylamino group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl (mercapto), sulfeno, sulfanilyl, sulfamyl, sulfamino, and phosphino, phosphinyl, phospho, phosphono and $-NR_aR_b$, wherein each of R_a and R_b may be the same or different and each is selected from the group consisting of hydrogen and optionally substituted: $C_{(1\cdot 20)}$ alkyl, $C_{(3\cdot 12)}$ cycloalkyl, $C_{(1\cdot 20)}$ alkenyl, $C_{(3\cdot 12)}$ cycloalkenyl, $C_{(1\cdot 20)}$ alkynyl, aryl, heteroaryl, and heterocyclic group;

R₂ and R₃ are independently selected from a unsubstituted or substituted member of the group consisting of methyl, ethyl, oxo, isopropyl, n-propyl, isobutyl, n-butyl, t-butyl, 2-hydroxyethyl, 3-hydroxypropyl, 3-hydroxy-n-butyl, 2-methoxyethyl, 4-methoxy-n-butyl, 5-hydroxyhexyl, 2-bromopropyl, 3-dimethylaminobutyl, 4-chloropentyl, methylamino, aminomethyl, and methylphenyl; and

 R_4 may be hydrogen or an optionally substituted member of the group consisting of $C_{(1-20)}$ alkyl, $C_{(3-12)}$ cycloalkyl, $C_{(3-12)}$ cycloalkenyl, $C_{(1-20)}$ alkynyl, aryl, heteroaryl, and heterocyclic group.

REMARKS

Reexamination and reconsideration in light of the foregoing amendment and following remarks is respectfully requested. Claims 1, 2 and 4-37 are pending in this application. Claim 3 has been canceled without prejudice or disclaimer thereof. Claims 1, 4, 6 and 34 have been amended to encompass infringing subject matter. A marked up version of the changes appears in Exhibit A attached hereto. No new matter has been added to the application.

In the Office Action Summary, the Examiner's consideration of the references cited in the Information Disclosure Statement filed October 9, 2001 is noted.

Claims 1-7 and 18-36 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite on the following 24 grounds.